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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/625,471	07/23/2003	Angel Pellicer	PELLICER1A	1686

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BROWDY AND NEIMARK, P.L.L.C.
624 Ninth Street, N.W.
Washington, DC 20001-5303

EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 09/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/625,471	PELLICER ET AL.	
	Examiner	Art Unit	
	Anne L. Holleran	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1-15 and 27-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16 and 19-26* is/are rejected.

7)☒ Claim(s) *17 and 18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/25/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group V (claims 16-26, 34 and 35) in the reply filed on 6/26/2006 is acknowledged. Applicant's remarks with respect to rejoining method groups under In re Ochiai is acknowledged.

2. Claims 1-35 are pending. Claims 1-15, and 27-33, drawn to non-elected inventions, are withdrawn from consideration.

Claims 16-26, 34 and 35 are examined on the merits.

3. Claim 16 is objected to for depending from a claim that is withdrawn from consideration. Claim 16 should be amended to recite the limitations of claim 1. Claims 19 and 20 are objected to for referring to elements of claim 1, which is claim that is withdrawn from consideration. If claim 16 is amended to include the limitations of claim 1, then the objection to claims 19 and 20 will be removed.

Claim Rejections - 35 USC § 112

4. Claims 16, 20, 34 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 16, 20, 34 and 35 are indefinite because they are drawn in part or in whole (claim 20) to nucleic acids that encode "naturally occurring variants" of an isolated polypeptide that is a

human Rgr protein and comprises the amino acid sequence of SEQ ID NO: 2. The specification fails to define the scope of structures that fall within boundaries of "naturally occurring variants of a human Rgr protein that comprises the amino acid sequence of SEQ ID NO: 2.

5. Claims 16, 19-26, 34 and 35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated nucleic acids that encode a polypeptide that comprises the amino acid sequence of SEQ ID NO: 2, or for nucleic acids *consisting of* nucleic acid sequences that encode SEQ ID NO: 8, or for specific nucleic acids *consisting of* the sequences of SEQ ID NOS: 5-7 and 9, 11, 13, 15, 17, 19, 21 and 23, does not reasonably provide enablement for nucleic acids encoding a polypeptide that is a fragment of SEQ ID NO: 2, or is any naturally occurring variant of SEQ ID NO: 2, or is any abnormally truncated variant, or is any alternative splice variant, or *comprises* nucleic acids that encode SEQ ID NO: 8, or *comprises* the nucleic acid sequences of SEQ ID NOS: 5-7 and 9, 11, 13, 15, 17, 19, 21 and 23. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

Claim 16 is drawn to nucleic acids that encode polypeptides comprising the amino acid sequence of SEQ ID NO: 2, comprising a fragment of SEQ ID NO: 2 and having the activity of human Rgr protein of SEQ ID NO: 2, and comprising a naturally occurring variant of a polypeptide comprising SEQ ID NO: 2. The specification fails to teach any specific activity for a polypeptide having the amino acid of SEQ ID NO: 2, because the specification fails to provide specific working examples demonstrating an activity of a protein that has the sequence of SEQ ID NO:2. Leonardi (Leonardi, P. et al., Oncogene, 21: 5108-5116, 2002, August) teaches that human rgr (a protein that encodes SEQ ID NO: 2) is homologous to RalGDS, which is a guanine nucleotide exchange factor that activates Ral GTPase by dissociating the bound GDP and allowing the binding of GTP, resulting in Ral activation. Leonardi also teaches that rabbit Rgr also dissociates GTP from Ral A. Additionally, rabbit Rgr induces phosphorylation of ERKs, p38 and JNK kinases and increases levels of GTP bound Ral and Ras (see Leonardi, page 5108, 2nd column). However, it is unpredictable whether rabbit Rgr and human Rgr will share exactly the same set of activities because the study of the relationship between the primary amino acid sequence and protein function is highly unpredictable. Bowie et al (Science, 247: 1306-1310, 1990) teaches that while it is known that many amino acid substitutions are possible in any given protein, the position with the protein sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Burgess et al (J. Cell Biology, 111: 2129-2138, 1990) teaches that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Lazar et al (Molecular and Cellular Biology, 8: 1247-1252, 1988) teaches that replacement of aspartic acid at position 47 with

alanine or asparagine does not affect biological activity while replacement with serine or glutamic acid sharply reduces the biological activity of the protein. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. Thus, given that the specification does not teach specific biological activities of human Rgr and it is unpredictable whether human Rgr exhibits exactly the same set if activities as rabbit Rgr, the claimed nucleic acids that are drawn to nucleic acid molecules that encode a fragment having the activity of human Rgr protein are not enabled by the specification, because one of skill in the art would first have to establish what are the activities of human Rgr. Without a set of activities to use in a routine assay, it would require further and undue experimentation to screen for useful fragments of human Rgr protein.

Furthermore, claims such as 20, 21 and 22 that are drawn to any variant or any alternative splice variant, or any abnormally truncated variant, without any specified activity, or without a showing that these variants may be used as markers or diagnostics, are also not enabled by the specification because one of skill in the art would not know how to use the claimed variants.

Claims 23-26 are drawn to nucleic acid molecules comprising nucleotides that encode fragments of SEQ ID NO: 2. Because of the use of the word "comprising", the claims encompass nucleic acid molecules encoding proteins for which a large portion of the protein is undescribed, and where the specification only teaches these fragments in the context of the whole protein and not in the context of any other species. Therefore, the claims are broadly drawn to generic nucleic acids, while the guidance provided by the specification is of only one example of a nucleic acid comprising the fragments. In view of the unpredictable nature of protein chemistry, and the breadth of the claims, as discussed above, one of skill in the art would

not know how to make and use a large majority of the genus encompassed by each of claims 23-26 without further and undue experimentation.

6. Claims 16 and 19-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that the specification fails to provide a description that is sufficient to support genus claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is for purposes of the 'written description' inquiry, "*whatever is now claimed*" (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed "nucleic acid molecules *comprising* a nucleotide sequence encoding for" a fragment of SEQ ID NO: 2, or naturally occurring variants or truncated variants of SEQ ID NO: 2, because the molecules encompassed contain undescribed regions. For a claim drawn to a genus, the written description requirement may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional

characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A "representative number of species" means that the species, which are adequately described, are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus (see Official Gazette 1241 OG 174, January 30, 2001). In the specification, fragments of SEQ ID NO: 2 are only taught in the specification in the context of SEQ ID NO: 2 itself, or in the context of the specific fragment itself (consisting of the fragment). Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for making or testing it. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112, is severable from its enablement provision. (See page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this

subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

7. Claims 16, 20, 34 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by D'Adamo (D'Adamo, et al., Oncogene, 14: 1295-1305, 1997; cited in the IDS) or Miller (Miller, M.J. et al., Journal of Biological Chemistry, 272(9): 5600-5605, 1997).

The claims are drawn to in part to nucleic acid molecules, vectors and cells transfected with a vector, where the nucleic acid molecules encode a polypeptide that is a naturally occurring variant of human Rgr, a polypeptide that comprises SEQ ID NO: 2. It is noted that the specification fails to provide a definition of what is encompassed by "naturally occurring variant".

D'Adamo teaches rabbit rgr protein and nucleic acid molecules that encode rabbit rgr, as well as vectors and cells transfected with the vector (see page 1299, 2nd column to page 1300 1st paragraph). Therefore, D'Adamo teaches nucleic acids, vectors and cells that are the same as that claimed. Miller teaches RalGDS, which is a protein related to human rgr, and nucleic acids that encode the C-terminal 98 amino acids of RalGDSb in a vector transfected into thyroid cells (see page 5600, 2nd column and 5602, 1st column). Therefore, Miller teaches nucleic acids, vectors and cells that are the same as that claimed.

7. Claims 16, 20, 22-25 are rejected under 35 U.S.C. 102(e) as being anticipated by WO 01/57278 (Penn et al., 9 August 2001).

Claims 16, 20 and 22-25 are drawn to nucleic acid molecules encoding variants of SEQ ID NO: 2, which variants include SEQ ID NO: 8 and nucleic acids having the sequence of SEQ ID NO: 5, 6 or 7.

Penn teaches nucleic acid molecules that comprise SEQ ID NO: 5, 6 or 7 and which encode SEQ ID NO: 8. Therefore, Penn teaches the claimed nucleic acid molecules.

8. Claims 16, 20, 22-25 are rejected under 35 U.S.C. 102(a) as being anticipated by Accession No. BI837800, (NIH-Mammalian Gene Collection, 04 Oct. 2001).

Claims 16, 20, 22-25 encompass variants such as nucleic acid molecules encoding SEQ ID NO: 8.

Accession No. BI837800 teaches nucleic acid molecules that comprises nucleic acid sequences that encode SEQ ID NO: 8. Therefore, Accession No. BI837800 teaches nucleic acid molecules that are the same as that claimed.

Conclusion

No claim is allowed. Claims 17 and 18 are objected for depending from a rejected claim.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the

status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
September 5, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER